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(54) Title: PROTEASE INHIBITORS

(57) Abstract

The present invention provides compounds of formula (I) which inhibit proteases, including cathepsin K, pharmaceutical compositions of such compounds, and methods for treating diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and rheumatoid arthritis; Paget's disease; hypercalcemia or malignancy; and metabolic bone disease therewith.

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PROTEASE INHIBITORS

FIELD OF THE INVENTION

This invention relates in general to heterocycleketohydrazide protease inhibitors, particularly such inhibitors of cysteine and serine proteases, more particularly compounds which inhibit cysteine proteases, even more particularly compounds which inhibit cysteine proteases of the papain superfamily, yet more particularly compounds which inhibit cysteine proteases of the cathepsin family, most particularly compounds which inhibit cathepsin K. Such compounds are particularly useful for treating diseases in which cysteine proteases are implicated, especially diseases of excessive bone or cartilage loss, e.g., osteoporosis, periodontitis, and arthritis.

BACKGROUND OF THE INVENTION

Bone is composed of a protein matrix in which spindle- or plate-shaped crystals of hydroxyapatite are incorporated. Type I Collagen represents the major structural protein of bone comprising approximately 90% of the structural protein. The remaining 10% of matrix is composed of a number of non-collagenous proteins, including osteocalcin, proteoglycans, osteopontin, osteonectin, thrombospondin, fibronectin, and bone sialoprotein. Skeletal bone undergoes remodeling at discrete foci throughout life. These foci, or remodeling units, undergo a cycle consisting of a bone resorption phase followed by a phase of bone replacement.

Bone resorption is carried out by osteoclasts, which are multinuclear cells of hematopoietic lineage. The osteoclasts adhere to the bone surface and form a tight sealing zone, followed by extensive membrane ruffling on their apical (i.e., resorbing) surface. This creates an enclosed extracellular compartment on the bone surface that is acidified by proton pumps in the ruffled membrane, and into which the osteoclast secretes proteolytic enzymes. The low pH of the compartment dissolves hydroxyapatite crystals at the bone surface, while the proteolytic enzymes digest the protein matrix. In this way, a resorption lacuna, or pit, is formed. At the end of this phase of the cycle, osteoblasts lay down a new protein matrix that is subsequently mineralized. In several disease states, such as osteoporosis and Paget's disease, the normal balance between bone resorption and formation is disrupted, and there is a net loss of bone at each cycle. Ultimately, this leads to weakening of the bone and may result in increased fracture risk with minimal trauma.

Several published studies have demonstrated that inhibitors of cysteine proteases are effective at inhibiting osteoclast-mediated bone resorption, and indicate an essential role for a cysteine proteases in bone resorption. For example, Delaisse, *et al.*, *Biochem. J.*, **1980**, *192*, 365, disclose a series of protease inhibitors in a mouse bone organ culture

system and suggest that inhibitors of cysteine proteases (e.g., leupeptin, Z-Phe-Ala-CHN_2) prevent bone resorption, while serine protease inhibitors were ineffective. Delaisse, *et al.*, *Biochem. Biophys. Res. Commun.*, **1984**, *125*, 441, disclose that E-64 and leupeptin are also effective at preventing bone resorption *in vivo*, as measured by acute changes in serum calcium in rats on calcium deficient diets. Lerner, *et al.*, *J. Bone Min. Res.*, **1992**, *7*, 433, disclose that cystatin, an endogenous cysteine protease inhibitor, inhibits PTH stimulated bone resorption in mouse calvariae. Other studies, such as by Delaisse, *et al.*, *Bone*, **1987**, *8*, 305, Hill, *et al.*, *J. Cell. Biochem.*, **1994**, *56*, 118, and Everts, *et al.*, *J. Cell. Physiol.*, **1992**, *150*, 221, also report a correlation between inhibition of cysteine protease activity and bone resorption. Tezuka, *et al.*, *J. Biol. Chem.*, **1994**, *269*, 1106, Inaoka, *et al.*, *Biochem. Biophys. Res. Commun.*, **1995**, *206*, 89 and Shi, *et al.*, *FEBS Lett.*, **1995**, *357*, 129 disclose that under normal conditions cathepsin K (which has also been called cathepsin O), a cysteine protease, is abundantly expressed in osteoclasts and may be the major cysteine protease present in these cells.

The abundant selective expression of cathepsin K in osteoclasts strongly suggests that this enzyme is essential for bone resorption. Thus, selective inhibition of cathepsin K may provide an effective treatment for diseases of excessive bone loss, including, but not limited to, osteoporosis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease. Cathepsin K levels have also been demonstrated to be elevated in chondroclasts of osteoarthritic synovium. Thus, selective inhibition of cathepsin K may also be useful for treating diseases of excessive cartilage or matrix degradation, including, but not limited to, osteoarthritis and rheumatoid arthritis. Metastatic neoplastic cells also typically express high levels of proteolytic enzymes that degrade the surrounding matrix. Thus, selective inhibition of cathepsin K may also be useful for treating certain neoplastic diseases.

Palmer, *et al.*, *J. Med. Chem.*, **1995**, *38*, 3193, disclose certain vinyl sulfones which irreversibly inhibit cysteine proteases, such as the cathepsins B, L, S, O2 and cruzain. Other classes of compounds, such as aldehydes, nitriles, a-ketocarbonyl compounds, halomethyl ketones, diazomethyl ketones, (acyloxy)methyl ketones, ketomethylsulfonium salts and epoxy succinyl compounds have also been reported to inhibit cysteine proteases. The synthesis of azatides (polyacylhydrazides) as peptide mimetics has recently been disclosed by Han and Janda, *J. Am. Chem. Soc.* **1996**, *118*, 2539.

The synthesis of N-phenyl-N'-(2-phenyloxazol-4-ylcarbonyl)hydrazide, as well as its N-(2,4-dinitrophenyl) derivative, have been described in Afridi, A., et al., *J. Chem. Soc, Perkin Trans. I*, **1976**, *3*, 315-20. Benko, A.,et al., *Justus Liebigs Ann. Chem.*, **1968**, *717*, 148-53 describes the preparation of N-(4-ethoxycarbonylthiazol-2-yl)-N'-[2-(4-pyridinyl)thiazol-4-ylcarbonyl]hydrazide.

Thus, a structurally diverse variety of cysteine protease inhibitors have been identified. However, these known inhibitors are not considered suitable for use as therapeutic agents in animals, especially humans, because they suffer from various shortcomings. These shortcomings include lack of selectivity, cytotoxicity, poor solubility, and overly rapid plasma clearance. A need therefore exists for methods of treating diseases caused by pathological levels of proteases, especially cysteine proteases, including cathepsins, especially cathepsin K, and for novel inhibitor compounds useful in such methods.

We have now discovered a novel class of heterocycleloketohydrazide compounds which are protease inhibitors, most particularly of cathepsin K.

SUMMARY OF THE INVENTION

An object of the present invention is to provide heterocycleketohydrazide protease inhibitors, particularly such inhibitors of cysteine and serine proteases, more particularly such compounds which inhibit cysteine proteases, even more particularly such compounds which inhibit cysteine proteases of the papain superfamily, yet more particularly such compounds which inhibit cysteine proteases of the cathepsin family, most particularly such compounds which inhibit cathepsin K, and which are useful for treating diseases which may be therapeutically modified by altering the activity of such proteases.

Accordingly, in the first aspect, this invention provides a compound according to Formula I.

In another aspect, this invention provides a pharmaceutical composition comprising a compound according to Formula I and a pharmaceutically acceptable carrier, diluent or excipient.

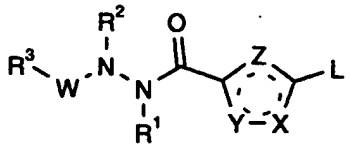
In yet another aspect, this invention provides intermediates useful in the preparation of the compounds of Formula I.

In still another aspect, this invention provides methods of treating diseases in which the disease pathology may be therapeutically modified by inhibiting proteases, particularly cysteine and serine proteases, more particularly cysteine proteases, even more particularly cysteine proteases of the papain superfamily, yet more particularly cysteine proteases of the cathepsin family, most particularly cathepsin K.

In a particular aspect, the compounds of this invention are especially useful for treating diseases characterized by bone loss, such as osteoporosis and gingival diseases, such as gingivitis and periodontitis, or by excessive cartilage or matrix degradation, such as osteoarthritis and rheumatoid arthritis.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides compounds of Formula I:



I

wherein:

L is C_{2-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $CH(R^4)NR^5R^6$, $CH(R^4)Ar$, $CH(R^4)OAr'$, or NR^4R^7;

Ar is phenyl or naphthyl, optionally independently substituted by one or more of Ph-C_{0-6}alkyl, Het-C_{0-6}alkyl, C_{1-6}alkyl, C_{1-6}alkoxy, Ph-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', or halogen. Two C_{1-6}alkyl groups may be combined to form a 5-7 membered ring, saturated or unsaturated, fused onto the Ar ring. Ph may be optionally substituted with one or more of C_{1-6}alkyl, C_{1-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', or halogen.

Ar' is phenyl or naphthyl, optionally independently substituted by one or more of Ph-C_{0-6}alkyl, Het-C_{0-6}alkyl, C_{1-6}alkyl, C_{1-6}alkoxy, Ph-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, or halogen. Ph may be optionally substituted with one or more of C_{1-6}alkyl, C_{1-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', or halogen. Two C_{1-6}alkyl groups may be combined to form a 5-7 membered ring, saturated or unsaturated, fused onto the Ar' ring.

Het is a stable 5- to 7-membered monocyclic or a stable 7- to 10-membered bicyclic heterocyclic ring, which is either saturated or unsaturated, and which consists of carbon atoms and from one to four heteroatoms selected from the group consisting of N, O and S, and wherein the nitrogen and sulfur heteroatoms may optionally be oxidized, and the nitrogen heteroatom may optionally be quaternized, and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The heterocyclic ring may be attached at any heteroatom or carbon atom which results in the creation of a stable structure, and may optionally be substituted with one or two moieties selected from the group consisting of Ph-C_{0-6}alkyl, Het-C_{0-6} alkyl, C_{1-6}alkyl, C_{1-6}alkoxy, Ph-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}$ NR^8R^9, $O(CH_2)_{1-6}NR^8R^9$, CO_2R'. Two C_{1-6}alkyl groups may be combined to form a 5-7 membered ring, saturated or unsaturated, fused onto the Het ring. Ph may be optionally substituted with one or more of C_{1-6}alkyl, C_{1-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', or halogen. Preferably, such heterocycles are selected from the group consisting of the piperidinyl,

piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, triazolyl, tetrazolyl, pyridyl, pyrazinyl, pryidazinyl, pyrimidinyl, triazinyl, tetrazinyl, oxazolidinyl, oxazolinyl, oxazolyl, isothiazolyl, isoxazolyl, morpholinyl, thiazolidinyl, thiazolinyl, thiazolyl, quinuclidinyl, indolyl, quinolinyl, isoquinolinyl, benzimidazolyl, benzopyranyl, benzoxazolyl, furyl, pyranyl, tetrahydrofuryl, tetrahydropyranyl, thienyl, benzoxazolyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, thiadiazolyl, and oxadiazolyl rings.

W is C(O) or SO_2;

X, Y, and Z are independently N, O, S or CR^{10}, provided that at least two of X, Y and Z are heteroatoms and at least one of X, Y and Z is N, or one of X, Y and Z is C=N, C=C or N=N and the other two are CR^{10} or N, further provided that at least two of X, Y and Z are N;

$\doteq$ indicates a single or double bond in the five-membered heterocycle;

R', R^1, R^2, R^5, R^8, R^9, R^{10}, and R^{12} are independently H, C_{1-6}alkyl, C_{2-6}alkenyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R^3 is C_{3-6}alkyl, Ar, Het, $CH(R^{11})Ar$, $CH(R^{11})OAr$, $NR^{11}R^{12}$, $CH(R^{11})NR^{12}R^{13}$; or

;

R^4, R^{11}, and R^{15} are independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-6}cycloalkyl-C_{0-6}-alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

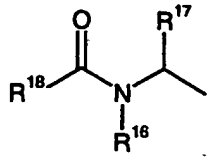
R^7 is C_{1-6}alkyl, C_{1-6}alkenyl, C_{3-6}cycloalkyl-C_{0-6}-alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl; R^4 and R^7 may be combined to form a 3-7 membered monocyclic or 7-10-membered bicyclic carbocyclic or heterocyclic ring, optionally independently substituted with 1-4 of C_{1-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, C_{1-6}alkoxy, Ar-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, or $O(CH_2)_{1-6}NR^8R^9$;

R^6 and R^{13} are R^{14}, $R^{14}C(O)$, $R^{14}C(S)$, $R^{14}OC(O)$, or $R^{14}OC(O)NR^9CH(R^{15})(CO)$; and

R^{14} is C_{1-6}alkyl, C_{2-6}alkenyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl.

Compounds of Formula I wherein Z = N, X = S, and Y = CH (thiazolo) are preferred. More preferred are such compounds wherein W is C(O). Even more preferred are such compounds wherein R^1 and R^2 are H.

Yet more preferred are such compounds wherein R^3 is:



wherein:

R^{16} is H or C_{1-6}alkyl, preferably H or Me;

R^{17} is C_{1-6}alkyl, C_{2-6}alkenyl, and C_{3-11}cycloalkyl-C_{1-6}alkyl, preferably *n*-propyl, *iso*-propyl, *iso*-pentyl, *tert*-butylmethyl, cyclopropylmethyl, *iso*-butyl, *n*-butyl, or allyl; and

R^{18} is C_{3-6}alkyl, OC_{3-6}alkyl, Ar, Het, $O(CH_2)_{0-3}$Ar, or $O(CH_2)_{0-3}$Het, preferably 2-pyridinylmethoxy, 3-pyridinylmethoxy, 4-pyridinylmethoxy, *tert*-butoxy, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-pyrazinyl, 4-*tert*-butoxycarbonylbenzyloxy, 4-carboxybenzyloxy, 3-*tert*-butoxycarbonylbenzyloxy, 3-carboxybenzyloxy, 2-methyl-3-pyridinylmethoxy, 6-methyl-3-pyridinylmethoxy, benzyloxy, 2-quinolino, 3-quinolino, 4-quinolino, 5-quinolino, 6-quinolino, 7-quinolino, 8-quinolino, 1-isoquinolino, 3-isoquinolino, piperidinyl, 4-methylpiperidinyl, 4-methylimidazol-5-yl, N-benzyl-pyrrolidinyl, N-methyl-pyrrolidinyl, 1-benzyl-5-methylimidazol-4-yl, 1-piperazinyl; 3-(2-pyridyl)benzyl, 2-methyl-3-pyridinyl, 2-methyl-4-pyridinyl, 6-methyl-3-pyridinyl, 4-dimethylaminobenzyloxy, 4-(4-morpholinomethyl)phenyl, 5-hydroxymethylimidazol-4-yl, 5-butyl-2-pyridinyl, 4-fluorophenyl, 3,4-difluorophenyl, 2-(1,8-naphthyridinyl), or 3,4-dimethoxyphenyl.

Also yet more preferred are compounds of Formula I wherein Z = N, X = S, and Y = CH (thiazolo), W is C(O), R^1 and R^2 are H, and wherein L is 4-(cis-2,6-dimethyl)-4-morpholinyl, N-cyclopropylmethyl-N-(2-methylpropyl)amino, 4-methyl-1-naphthyl, N-methyl-N-(2-methylpropyl)amino, 1-naphthyl, 5-acenaphthyl, N-cyclopropyl-N-cyclopropylmethylamino, N,N-bis-(2-methylpropyl)amino, 1-(1,2,3,4-tetrahydroquinolino, N-cyclopropylmethyl-N-propylamino, N-(2-methylpropyl)-N-phenylamino, 2-methoxy-1-naphthyl, 2-benzyloxyphenyl, 2-benzyloxy-1-naphthyl, 9-phenanthrenyl, 9-anthracenyl, phenyl, 2-(4-*tert*-butoxycarbonyl)benzyloxyphenyl, 2-(4-carboxybenzyloxy)phenyl, N-cyclopropylamino, 8-quinolino, N,N-bis-(cyclopropylmethyl)amino, 4-(2,2-dimethylaminoethoxy)-1-naphthyl, or 1-(N-benzyloxycarbonylamino)-3-methylbutyl.

The following compounds are particularly preferred embodiments of the present invention:

N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(4-methyl-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(5-acenaphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-[1-(1,2,3,4-tetrahydroquinolino)]thiazol-4-ylcarbonyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[4-methyl-2-(3-phenyl)phenylpent-4-enoyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropylmethyl-N-propylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[4-methyl-2-(3-phenyl)phenylpentanoyl]hydrazide;
N-[N-(2-methylpropyl)-N-(3-phenylphenyl)carbamoyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[4-methyl-2-(3-phenyl)phenylpentanoyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[4-methyl-2-(3-phenyl)phenylpentanoyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;
N-[2-(2-methoxy-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[4-methyl-2-(3-phenyl)phenylpentanoyl]hydrazide;
N-[2-(2-benzyloxy-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-(9-phenanthrenyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-(9-anthracenyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-(-*tert*-butoxycarbonyl-L-leucinyl)ydrazide;
N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(L-leucinyl)]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;
N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyrazinecarbonyl)-L-leucinyl]hydrazide;
N-[N,N-bis-(2-methylpropyl)carbamoyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;
N-(2-phenylthiazol-4-ylcarbonyl)-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-[2-(4-*tert*-butoxycarbonyl)benzyloxyphenyl]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[2-(4-carboxybenzyloxy)phenyl]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-carboxybenzyloxycarbonyl)-L-leucinyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycaronyl-L-leucinyl)-N'-[2-[2-(4-*tert*-butoxycarbonyl)benzyloxyphenyl]thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycaronyl-L-leucinyl)-N'-[2-[2-(4-carboxybenzyloxy)phenyl]thiazol-4-ylcarbonyl]hydrazide;

N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-()-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

Example 61

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide

Following the procedure of Example 59(a)-59(c), except substituting picolinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.086 g, 54%). MS (ESI): 488.3 $(M+H)^+$.

Example 62

Preparation of N-[N-(3-carboxybenzyloxycarbonyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of 4(c), except substituting N-[N-(3-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-Methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucine *tert*butoxycarbonyl ester, the title compound was prepared as a white solid (21 mg, 93%). MS (ESI): 544.3 $(M+H)^+$.

Example 63

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 2-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.123 g, 80%). MS (ESI): 538.2 $(M+H)^+$.

Example 64

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 3-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.109 g, 77%). MS (ESI): 538.2 $(M+H)^+$.

Example 65

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-methylpiperidinecarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 1-methylpiperidine-4-carboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.059 g, 45%). MS (ESI): 508.2 $(M+H)^+$.

Example 66

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 4-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.096 g, 68%). MS (ESI): 538.3 $(M+H)^+$.

Example 67

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(5-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 5-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.089 g, 63%). MS (ESI): 538.3 $(M+H)^+$.

Example 68

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 7-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.106 g, 75%). MS (ESI): 538.2 $(M+H)^+$.

Example 69

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(6-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 6-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.111 g, 79%). MS (ESI): 538.2 $(M+H)^+$.

Example 70

Preparation of N-[N-(1-isoquinolinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 1-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.076 g, 54%). MS (ESI): 538.2 $(M+H)^+$.

Example 71

Preparation of N-[N-(3-isoquinolinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 3-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.055 g, 39%). MS (ESI): 538.2 $(M+H)^+$.

Example 72

Preparation of N-[N-(4-methylimidazol-5-ylcarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) 4-methylimidazole-5-carboxylic acid

Following the procedure of Example 1(g), except substituting ethyl 4-methylimidazole-5-carboxylate for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid (0.428 g, 52%). MS (ESI): 126.8 $(M+H)^+$.

b) N-[N-(4-methylimidazol-5-ylcarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(h), except substituting N-(L-leucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide and 4-methylimidazole-5-carboxylic acid for N-(4-pyridinylmethoxycarbonyl)-L-leucine, the title compound was prepared as a white solid (0.108 g, 84%). MS (ESI): 491.3 $(M+H)^+$.

Example 73

Preparation of N-(N-benzyl-L-prolinyl-L-leucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-benzyl proline for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.075 g, 50%). MS (ESI): 570.2 $(M+H)^+$.

Example 74

Preparation of N-[N-(1-benzyl-5-methylimidazol-4-ylcarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 72(a)-72(b), except substituting 1-benzyl-5-methylimidazole-4-carboxylic acid for 4-methylimidazole-5-carboxylic acid in step (a), the title compound was prepared as a white solid (0.115 g, 75%). MS (ESI): 581.1 $(M+H)^+$.

Example 75

Preparation of N-[N-(3-methylisonicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) 4-cyano-2-methylpyridine

To neat picoline N-oxide (10.0 g, 91.7 mmol) at room temperature was added iodoethane (51.5 g, 330 mmol) dropwise. After standing for 24 h, the salt was filtered off and washed with ether. The solid was dissolved in ethanol/water (70 mL/30 mL) and potassium cyanide (11.0 g, 172 mmol) in water (31 mL) was added dropwise over 100 min at 48-50 °C. After the addition was complete, the solution continued stirring at the same temperature for 30 min. The solution was then extracted with chloroform. The organic layer was washed with brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane) to yield the title compound as a pale yellow oily solid (3.9 g, 36%). MS (ESI): 118.8 $(M+H)^+$.

b) 2-methylpyridine-4-carboxylic acid

The compound of Example 75(a) (0.300 g, 2.5 mmol) was dissolved in concentrated hydrochloric acid (3 mL). After stirring at reflux for 18 h, the solution was concentrated to yield the title compound as a white solid (0.342 g, 100%). MS (ESI): 137.8 $(M+H)^+$.

c) N-[N-(3-methylisonicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(h), except substituting N-(L-leucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide and 2-methylpyridine-4-carboxylic acid for N-(4-pyridinylmethoxycarbonyl)-L-leucine, the title compound was prepared as a white solid (0.095 g, 72%). MS (ESI): 502.2 $(M+H)^+$.

Example 76

Preparation of N-[2-(N-cyclopropylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 1(a)-1(h), except substituting cyclopropylamine for cis-2,6-dimethylmorpholine in step (a) and 2-pyridylcarbinol for 4-pyridylcarbinol in step (f), the title compound was prepared as a white solid (140 mg, 50%). MS (ESI): 447.3 $(M+H)^+$.

Example 77

Preparation of N-[N-(2-benzoxazolyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

A solution of the compound of Example 59(c) (100 mg, 0.26 mmol), 2-chlorobenzoxazole (40.2 mg, 0.26 mmol, 0.03 mL) and triethylamine (26.5 mg, 0.26 mmol, 0.365 mL) in 1:1 THF/methanol (1 mL) was heated at 60 °C for 48 h. The solution was diluted with ethyl acetate, washed with saturated aqueous $NaHCO_3$, water (2 X) and saturated brine, then dried ($MgSO_4$), filtered and concentrated. The residue was purified by flash chromatography on 4 g of 230-400 mesh silica gel, eluting with 1:1 ethyl acetate/hexanes, to give the title compound as a pale yellow solid (50.2 mg, 38%). MS (ESI): 500.2 $(M+H)^+$.

Example 78

Preparation of N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-[N,N-bis-(2-methylpropyl)amino]oxazol-4-ylcarbonyl]hydrazide

a) N,N-diisobutylurea

A solution of diisobutylamine (4.5 g, 34.8 mmol, 6.08 mL) and chlorosulfonyl isocyanate (4.93 g, 34.8 mmol, 3.03 mL) in THF (200 mL) was allowed to stir at room temperature for 20 min, then water (10 mL) was added and the solution was allowed to stir at room temperature for 17 h. The solution was concentrated, the residue was redissolved in ethyl acetate, washed with water, saturated aqueous $NaHCO_3$ and saturated brine, then dried ($MgSO_4$), filtered and concentrated to give the title compound as a colorless oil which crystallized upon standing (6.0 g, 100%). MS (ESI): 173.3 $(M+H)^+$.

b) N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-[N,N-bis-(2-methylpropyl)amino]oxazol-4-ylcarbonyl]hydrazide

Following the procedure of Examples 1(c)-1(d) and 1(h), except substituting N,N-diisobutylurea for cis-2,6-dimethyl-4-morpholinothiourea in step (c) and N-benzyloxycarbonyl-L-leucine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as a white solid (126 mg, 64%). MS (ESI): 502.3 $(M+H)^+$.

Example 79

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

a) N-cyclopropyl isobutylamine

Following the procedure of Example 9(a), except substituting isobutyraldehyde for cyclopropane carboxaldehyde, the title compound was prepared as a colorless oil (1.9 g, 58%). MS (ESI): 113.9 $(M+H)^+$.

b) N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 1(a)-1(h), except substituting N-cyclopropyl isobutylamine for cis-2,6-dimethylmorpholine in step (a) and 2-pyridyocarbinol for 4-pyridylcarbinol in step (f), the title compound was prepared as a white solid (150 mg, 69% yield). MS (ESI): 503.2 $(M+H)^+$.

Example 80

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 4(a)-4(d), except substituting 2-pyridylcarbinol for 4-pyridylcarbinol in step (a) and N-cyclopropyl isobutylamine for N-methyl isobutylamine in step (d), the title compound was prepared as a white solid (85 mg, 32%). MS (ESI): 517.3 $(M+H)^+$.

Example 81

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(1-piperazinecarbonyl)-L-leucinyl]hydrazide

a) N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-*tert*-butoxycarbonyl-1-piperazinecarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 23(c), except substituting N-*tert*-butoxycarbonylpiperazine for N-(3-phenyl)phenyl isobutylamine, the title compound was prepared as a white solid (131 mg, 85%). MS (ESI): 595.2 $(M+H)^+$.

b) N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(1-piperazinecarbonyl)-L-leucinyl]hydrazide

Following the procedure of 4(c), except substituting N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-*tert*-butoxycarbonyl-1-piperazinecarbonyl)-L-leucinyl]hydrazide for N-Methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucine *tert*butoxycarbonyl ester, the title compound was prepared as a white solid (47 mg, 54%). MS (ESI): 495.2 $(M+H)^+$.

Example 82

Preparation of N-[4-methyl-2-(4-phenoxy)phenylpentanoyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 17(a)-17(c), except substituting 4-phenoxyphenylacetic acid for 4-phenoxyphenylacetic acid in step (a), the title compound was prepared as a white solid (134 mg, 67%). MS (ESI): 536.2 $(M+H)^+$.

Example 83

Preparation of N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

a) bis-(cyclopropylmethyl)amine

Following the procedure of Example 9(a), except substituting aminomethylcyclporopane for cyclopropylamine, the title compound was prepared as a colorless liquid (2.5 g, 96%). MS (ESI): 125.8 $(M+H)^+$.

b) N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 1(a)-1(h), except bis-(cyclopropylmethyl)amine for cis-2,6-dimethylmorpholine in step (a) and 2-pyridyocarbinol for 4-pyridylcarbinol in step (f), the title compound was prepared as a yellow solid (115 mg, 30%). MS (ESI): 515.3 $(M+H)^+$.

Example 84

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 2-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (125 mg, 59%). MS (ESI): 521.2 $(M+H)^+$.

Example 85

Preparation of N-[N-(8-quinolinoyl)-L-leucinyl]-N'-[2-(8-quinolinyl)thiazol-4-ylcarbonyl]hydrazide

a) N-[2-(8-quinolinyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 3(a)-3(f), except substituting 8-bromoquinoline for 1-bromo-4-methylnaphthalene in step (d), the title compound was prepared as a pale yellow solid (0.306 g, 100%). MS (ESI): 271.2 $(M+H)^+$.

b) N-[N-(8-quinolinoyl)-L-leucinyl]-N'-[2-(8-quinolinyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(b)-59(d), except substituting N-[2-(8-quinolinyl)thiazol-4-ylcarbonyl]hydrazide for N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide in step (b), the title compound was prepared as a white solid (0.111 g, 66%). MS (ESI): 539.2 $(M+H)^+$.

Example 86

Preparation of N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Examples 3(a)-3(c) and 3(e)-3(g), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthalene boronic acid in step (e) and N-benzyloxycarbonyl-L-leucine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (g), the title compound was prepared as a white solid (0.145 g, 60%). MS(ESI): 517.3 $(M+H)^+$.

Example 87

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 3-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (150 mg, 75%). MS (ESI): 521.2 $(M+H)^+$.

Example 88

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 3-isoquinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (187 mg, 82%). MS (ESI): 521.1 $(M+H)^+$.

Example 89

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 6-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (155 mg, 59%). MS (ESI): 521.3 $(M+H)^+$.

Example 90

Preparation of N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 83(a)-83(b), except substituting 2-methyl-3-pyridylcarbinol for 2-pyridylcarbinol in step (b), the title compound was prepared as a yellow solid (105 mg, 46%). MS (ESI): 529.3 $(M+H)^+$.

Example 91

Preparation of N-(N-benzyloxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) N-benzyloxycarbonyl-L-b-*tert*-butylalanine

To a stirring solution of L-b-*tert*-butylalanine (1.0 g, 6.89 mmol) in water (2.1 mL) and 5 N NaOH (1.38 mL) at 0 °C was added benzyl chloroformate (1.3 g, 7.58 mmol) and 2 N NaOH (3.8 mL) in ten alternating portions, over 1.5 h. After the additions are complete the mixture was stirred for another 30 min. at room temperature. The pH is then taken to 10 and the mixture is extracted with ether (50 mL). The aqueous layer was acidified to pH 3 with 3 N HCl and extracted with ether (3 x 50 mL). The organic layers are combined, dried ($MgSO_4$), filtered and concentrated to yield the title compound as a colorless oil (1.59 g, 83%). MS(ESI): 278.2 $(M+H)^-$.

b) N-(N-benzyloxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Examples 3(a)-3(c) and 3(e)-3(g), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthalene boronic acid in step (e) and N-benzyloxycarbonyl-L-*tert*-butylalanine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (g), the title compound was prepared as a white solid (0.214 g, 87%). MS (ESI): 531.3 $(M+H)^+$.

Example 92

Preparation of N-(N-benzyloxycarbonyl-L-cyclopropylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) N-benzyloxycarbonyl-L-allylglycine

Following the procedure of Example 91(a), except substituting L-allylglycine for L-*tert*-butylalanine, the title compound was prepared.

b) N-benzyloxycarbonyl-L-cyclopropylalanine methyl ester

Diazomethane (4.8 mmol in 18 ml Et_2O) was added to a solution of the compound of Example 92(a) (0.210 g, 0.48 mmol) in 1 ml Et_2O at room temperature and was stirred for 5 minutes. Then $Pd(OAc)_2$ (2 mg) was added and the reaction was stirred overnight, filtered through silica gel, concentrated *in vacuo*, and was used in the next reaction without further purification (205 mg, 95%). MS (ESI): 300.1 $(M+Na)^+$.

c) N-benzyloxycarbonyl-L-cyclopropylalanine

Following the procedure of Example 1(g) except substituting N-benzyloxycarbonyl-L-cyclopropylalanine methyl ester for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid (165 mg, 82%). MS (ESI): 264.2 $(M+H)^+$.

d) N-(N-benzyloxycarbonyl-L-cyclopropylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Examples 3(a)-3(c) and 3(e)-3(g), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthalene boronic acid in step (e) and N-benzyloxycarbonyl-(L)-*tert*-butylalanine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (g), the title compound was prepared as a white solid (0.054 g, 67%). MS (ESI): 515.2 $(M+H)^+$.

Example 93

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-[3-(2-pyridyl)phenylacetyl]-L-leucinyl]hydrazide

a) methyl 3-9trifluoromethanesulfonyloxyphenylacetate

To an oven-dried flask under Argon atmosphere containing sodium hydride (2.54 g, 60% dispersion in mineral oil, 63.5 mmol) was added anhydrous pentane (20 mL). The slurry was stirred for 5 min, allowed to settle, most of the pentane was removed, and anhydrous THF (40 mL) was added. To this suspension was added a solution of methyl 3-hydroxyphenylacetate (9.99 g, 60.1 mmol) in anhydrous THF (20 mL) and the reaction was stirred at room temperature for 20 min. To this mixture was then added a solution of N-phenyltrifluoromethanesulfonimide (22.53 g, 63.1 mmol)) in anhydrous THF (40 mL) and the reaction was stirred at room temperature until TLC analysis indicated the complete consumption of starting material (1.5 h). The reaction was quenched by the addition of H_2O (10 mL), concentrated to one half original volume, then diluted with $CHCl_3$ (200 mL) and washed with H_2O. The aqueous layer was washed with fresh $CHCl_3$ (50 mL), the combined organic layers were washed with 10% Na_2CO_3, H_2O, and brine, then dried (MgSO4), filtered and concentrated. Column chromatography of the residue (silica gel, 5:95 EtOAc: hexanes, then 10:90 EtOAc: hexanes) gave 17.47 g of the title compound. ^1H NMR (400 MHz, $CDCl_3$) d 7.42 (m, 1H), 7.31-7.19 (m, 3H), 3.72 (s, 3H), 3.68 (s, 2H).

b) methyl 3-(2-pyridyl)phenylacetate

To a solution of the compound of Example 93(a) (6.86 g, 23.0 mmol) in anhydrous dioxane (100 mL) was added 2-pyridylstannane (8.89 g, 24.1 mmol), LiCl (2.94 g, 69.3 mmol), 2,6-di-tert-butyl-4-methylphenol (a few crystals), and $Pd(PPh_3)_4$ (632.1 mg, 0.55 mmol). The reaction was protected from light with foil and heated to reflux overnight. The reaction was allowed to cool to room temperature and concentrated. Column chromatography of the residue (silica gel, 1:3 EtOAc: hexanes, then 1:2 EtOAc: hexanes) gave 3.85 g of the title compound: MS (ESI): 228.1 $(M+H)^+$.

c) 3-(2-pyridyl)phenyl acetic acid

Following the procedure of Examples 1(g), except substituting methyl 3-(2-pyridyl)phenylacetate for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared. MS (ESI): 214.3 $(M+H)^+$.

e) N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-[3-(2-pyridyl)phenylacetyl]-L-leucinyl]hydrazide

Following the procedure of Examples 3(a)-3(c) and 3(e)-3(g), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthalene boronic acid in step (e) and 3-(2-pyridyl)phenylacetic acid for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (g), the title compound was prepared as a white solid (0.149 g, 79%). MS (ESI): 578.1 $(M+H)^+$.

Example 94

Preparation of N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-picolinyl-L-leucinyl)hydrazide

a) N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide

Following the procedure of Example 1(a)-1(d) and 1(h), except substituting bis-(cyclopropylmethyl)amine cyclopropylamine for cis-2,6-dimethylmorpholine in step (a) and N-*tert*-butoxycarbonyl-L-leucine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as an orange oil. MS (ESI): 480.3 $(M+H)^+$.

b) N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-picolinyl-L-leucinyl)hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a), the title compound was prepared as a yellow solid (74 mg, 41%). MS (ESI): 485.3 $(M+H)^+$.

Example 95

Preparation of N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(a)-1(d) and 1(h), except substituting bis-(cyclopropylmethyl)amine for cis-2,6-dimethylmorpholine in step (a) and N-bejnzyloxycarbonyl L-leucine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as as a yellow solid (140 mg, 69%). MS (ESI): 514.3 $(M+H)^+$.

Example 96

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-leucinyl]hydrazide

a) 6-methylnicotinic acid

Following the procedure of Example 1(g), except substituting methyl-6-methylnicotinate for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid (506 mg, 100%). MS (ESI): 137.9 $(M+H)^+$.

b) N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylnicotinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 6-methylnicotinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (150 mg, 41%). MS (ESI): 485.4 $(M+H)^+$.

Example 97

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-methylnicotinoyl)-L-leucinyl]hydrazide

a) 2-methylnicotinic acid

Following the procedure of Example 1(g), except substituting methyl-2-methylnicotinate for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid (1.6 g, 100%). MS (ESI): 138.2 $(M+H)^+$.

b) N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-methylnicotinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 2-methylnicotinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (170 mg, 71%). MS (ESI): 485.3 $(M+H)^+$.

Example 98

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-methylisonicotinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 2-methylpyridine-4-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (120 mg, 57%). MS (ESI): 485.2 $(M+H)^+$.

Example 99

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 8-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (200 mg, 94%). MS (ESI): 521.2 $(M+H)^+$.

Example 100

Preparation of N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 8-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a yellow solid (25 mg, 12%). MS (ESI): 535.3 $(M+H)^+$.

Example 101

Preparation of N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-

leucinyl)hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 3-isoquinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a yellow solid (25 mg, 10%). MS (ESI): 535.3 $(M+H)^+$.

Example 102

Preparation of N-[2-[4-(2,2-dimethylaminoethoxy)-1-naphthyl]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide

a) 4-bromo-1-naphthol

To a vigorously stirred suspension of 1,4-dibromonaphthalene (15.3 g, 53.7 mmol) in hexane/THF (300 mL) at -78 °C was added n-butyllithium (22.3 mL, 56.4 mmol, 2.5 M in hexane) dropwise. After stirring for an additional 30 min. at -78 °C, bis(trimethylsilyl)peroxide (11 g, 61.8 mmol) [Taddei, M., Ricci, A., *Synthesis*, 1986, 633] was added slowly via syringe. After warming to room temperature and stirring an additional 3 h, the mixture was diluted with ethyl acetate and washed with 1 N HCl then brine. The organic layer was dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography (silica gel, ethyl acetate/hexane) to yield the title compound as an off-white solid (6.5 g, 54%). MS (ESI): 221.1 $(M+H)^-$.

b) 4-bromo-1-naphthyl *tert*-butyl ether

Following the procedure of Example 39(a), except substituting 4-bromo-1-naphthol for 4-bromomethylbenzoic acid, the title compound was prepared as a colorless oil (2.34 g, 62%). ^1H NMR (400 MHz, $CDCl_3$) d 8.28 (d, 1H), 8.18 (d, 1H), 7.67 (d, 1H), 7.60 (t, 1H), 7.54 (t, 1H), 7.01 (d, 1H), 1.51 (s, 9H).

c) ethyl 2-(4-*tert*-butoxy-1-naphthyl)thiazole-4-carboxylate

Following the procedure of Example 3(a)-3(e), except substituting 4-bromo-1-naphthyl *tert*-butyl ether for 1-bromo-4-methylnaphthalene in step (d), the title compound was prepared as a white solid (0.783 g, 67%). MS (ESI): 356.2 $(M+H)^+$.

d) ethyl 2-(4-hydroxy-1-naphthyl)thiazole-4-carboxylate

Following the procedure of 4(c), except substituting ethyl 2-(4-*tert*-butoxy-1-naphthyl)thiazole-4-carboxylate for N-Methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucine *tert*butoxycarbonyl ester, the title compound was prepared as a yellow solid (0.580 g, 88%). MS (ESI): 300.1 $(M+H)^+$.

e) ethyl 2-[4-(2-N,N-dimethylaminoethoxy)-1-naphthyl]thiazole-4-carboxylate

Following the procedure of Example 28(d), except substituting ethyl 2-(4-hydroxy-1-naphthyl)thiazole-4-carboxylate for ethyl 2-(2-hydroxy-1-naphthyl)thiazole-4-carboxylate and 2-(N,N-dimethylamino)ethanol for benzyl alcohol, the title compound was prepared as a white solid (0.097 g, 52%). MS (ESI): 371.3 $(M+H)^+$.

f) N-(8-quinolinoyl)-L-leucine methyl ester

Following the procedure of Example 1(h), except substituting L-leucine methyl ester hydrochloride for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide and 8-quinoline carboxylic acid for N-(4-pyridylmethoxycarbonyl)-L-leucine, the title compound was prepared as a white solid (0.637 g, 41%). MS (ESI): 301.2 $(M+H)^+$.

g) N-(8-quinolinoyl)-L-leucine

Following the procedure of Example 1(g), except substituting N-(8-quinolinoyl)-L-leucine methyl ester for N-(4-pyridylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid (0.150 g, 25%). ^1H NMR (400 MHz, $CDCl_3$) d 8.89 (t, 1H), 8.78 (d, 1H), 8.21 (d, 1H), 7.90 (d, 1H), 7.57 (t, 1H), 7.43 (t, 1H), 4.88 (m, 1H), 1.92 (m, 3H), 1.03 (m, 6H).

h) N-[2-[4-(2,2-dimethylaminoethoxy)-1-naphthyl]thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(d), except substituting ethyl 2-[4-(2-N,N-dimethylaminoethoxy)-1-naphthyl]thiazole-4-carboxylate for ethyl 2-(cis-2,6-dimethyl-4-morpholino)thiazole-4-carboxylate, the title compound was prepared as a yellow solid (0.091 g, 100%). MS (ESI): 357.2 $(M+H)^+$.

i) N-[2-[4-(2,2-dimethylaminoethoxy)-1-naphthyl]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 1(h), except substituting N-[2-[4-(2,2-dimethylaminoethoxy)-1-naphthyl]thiazol-4-ylcarbonyl]hydrazide for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide and N-(8-quinolinoyl)-L-leucine for N-(4-pyridylmethoxycarbonyl)-L-leucine, the title compound was prepared as a yellow solid (0.050g, 31%). MS (ESI): 625.2 $(M+H)^+$.

Example 103

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 7-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (100 mg, 50%). MS (ESI): 521.2 $(M+H)^+$.

Example 104

Preparation of N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 6-methylnicotinic acid for picolinic acid in step (b), the title compound was prepared as a yellow solid (40 mg, 15%). MS (ESI): 499.3 $(M+H)^+$.

Example 105

Preparation of N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-methyl-L-prolinyl-L-leucinyl)hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-methyl-L-proline for picolinic acid in step (b), the title compound was prepared as a white solid (62 mg, 48%). MS (ESI): 477.3 $(M+H)^+$.

Example 106

Preparation of N-(N-benzyloxycarbonyl-L-norvalinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Examples 3(a)-3(c) and 3(e)-3(g), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthalene boronic acid in step (e) and N-

benzyloxycarbonyl-L-norvaline for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (g), the title compound was prepared as a white solid (180 mg, 96%). MS (ESI): 503.2 $(M+H)^+$.

Example 107

Preparation of N-(N-benzyloxycarbonyl-L-isoleucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Examples 3(a)-3(c) and 3(e)-3(g), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthalene boronic acid in step (e) and N-benzyloxycarbonyl-L-isoleucine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (g), the title compound was prepared as a white solid (167 mg, 87%). MS (ESI): 517.1 $(M+H)^+$.

Example 108

Preparation of N-[N-(4-dimethylaminomethylbenzoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) methyl 4-(N,N-dimethylaminomethyl)benzoate

Methyl 4-(bromomethyl)benzoate (2.0 g, 8.73 mmol) was added to a saturated solution of dimethylamine in methanol. After stirring for 25 min, the solution was concentrated and the residue was partitioned between 1N NaOH and ethyl acetate. The organic layer was washed with saturated brine, dired ($MgSO_4$), filtered, and concentrated to provide the title compound as a colorless liquid (1.67 g, 99%). ^1H NMR (250 MHz, $CDCl_3$) d 8.00 (d, 2H), 7.39 (d, 2H), 3.91 (s, 3H), 3.47 (d, 2H), 2.25 (s, 6H).

b) 4-(N,N-dimethylaminomethyl)benzoic acid

Following the procedure of Example 1(g), except substituting methyl 4-(N,N-dimethylaminomethyl)benzoate for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid (1.6 g, 100%). ^1H NMR (400 MHz, CD_3OD) d 7.94 (d, 2H), 7.36 (d, 2H), 3.64(s, 2H), 2.35 (s, 6H).

c) N-[N-(4-dimethylaminomethylbenzoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 4-(N,N-dimethylaminomethyl)benzoic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (87 mg, 61%). MS (ESI): 544.2 $(M+H)^+$.

Example 109

Preparation of N-(N-benzyloxycarbonyl-L-norleucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Examples 3(a)-3(c) and 3(e)-3(g), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthalene boronic acid in step (e) and N-benzyloxycarbonyl-L-norleucine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (g), the title compound was prepared as a white solid (184 mg, 96%). MS (ESI): 517.1 $(M+H)^+$.

Example 110

Preparation of N-[N-(4-dimethylaminomethylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) 4-(N,N-dimethylamino)benzyl alcohol

To a stirring solution of the compound of Example 108(a) (1.63 g, 8.4 mmol) in 25 mL of ether, cooled to 0 °C, was added dropwise a 1 M solution of lithium aluminum hydride (8.4 mmol, 8.4 mL). After 5 min, the reaction was quenched by the addition of water (0.33 mL), 15% aqueous NaOH (0.33 mL) and water (1.0 mL). The precipitate was removed by filtration, washed with ether 2 times and the filtrate was concentrated to provide the title compound as a colorless oil (1.36 g, 98%). ^1H NMR (250 MHz, $CDCl_3$) d 7.32 (d, 2H), 7.28 (d, 2H), 4.68 (s, 2H), 3.41 (s, 2H), 2.22 (s, 6H).

b) N-[N-(4-dimethylaminomethylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(e)-1(h), except substituting 4-(N,N-dimethylamino)benzyl alcohol for 4-pyridylcarbinol in step (f) and N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide, the title compound was prepared as a white solid (186 mg, 87%). MS (ESI): 574.3 $(M+H)^+$.

Example 111

Preparation of N-(N-benzyloxycarbonyl-L-norvalinyl)-N'-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 27(a)-27(c), except substituting N-benzyloxycarbonyl-L-norvaline for 2-(3-phenylphenyl)-4-methylpentanoic acid in step (c), the title compound was prepared as a white solid. MS (ESI): 559.0 $(M+H)^+$.

Example 112

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 4-methylimidazole-5-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (100 mg, 65%). MS (ESI): 474.3 $(M+H)^+$.

Example 113

Preparation of N-[N-[4-(4-morpholinomethyl)benzoyl]-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 108(a)-108(c), except substituting morpholine for dimethylmaine in step (a), the title compound was prepared as a white solid (0.097 g, 51%). MS (ESI): 586.2 $(M+H)^+$.

Example 114

Preparation of N-[N-(2-methylnicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 2-methylnicotinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.103 g, 60%). MS (ESI): 502.2 $(M+H)^+$.

Example 115

Preparation of N-[N-(6-methylnicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 6-methylnicotinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.134 g, 79%). MS (ESI): 502.2 $(M+H)^+$.

Example 116

Preparation of N-[N-(4-methylimidazol-5-ylcarbonyl)-L-allylglycinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) N-*tert*-butoxycarbonyl-L-allylglycine

To a stirring solution of L-allylglycine (6.28 g, 54.5 mmol) in dioxane/water/1 N NaOH (110 mL/55 mL/55 mL) at 0 °C was added di-*tert*-butyl dicarbonate (12.5 g, 57.2 mmol). After stirring for 30 min., the solution was concentrated and redissolved in 60 mL of water. A layer of ethyl acetate was added and the aqueous layer was acidified to pH 3 with 0.3 N $KHSO_4$. The aqueous layer was extracted with ethyl acetate (2 X). The organic layers were combined, washed with water (2 X), dried ($MgSO_4$), filtered and concentrated to yield the title compound as a white solid (10.11 g, 86%). MS (ESI): 453.2 $(2M+Na)^+$.

b) N-[N-(4-methylimidazol-5-ylcarbonyl)-L-allylglycinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-allylglycine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 4-methylimidazole-5-carboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.112 g, 67%). MS (ESI): 475.1 $(M+H)^+$.

Example 117

Preparation of N-(N-b-*tert*-butoxycarbonyl-L-*tert*-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide

a) N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine

Following the procedure of Example 116(a), except substituting L-*tert*-butylalanine for L-allylglycine, the title compound was prepared as a white solid (2.36 g, 70%). MS(ESI): 268.3 $(M+Na)^+$.

b) N-(N-b-*tert*-butoxycarbonyl-L-tert-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(a)-1(d) and 1(h), except substituting N-cyclopropylmethyl cyclopropylamine for cis-2,6-dimethylmorpholine in step (a) and N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as a white solid (0.96 g, 100%). MS (ESI): 480.3 $(M+H)^+$.

Example 118

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-b-*tert*-butoxycarbonyl-L-tert-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 8-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (160 mg, 82%). MS (ESI): 535.3 $(M+H)^+$.

Example 119

Preparation of N-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 4-methylimidazole-5-carboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.096 g, 58%). MS (ESI): 505.2 $(M+H)^+$.

Example 120

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-b-*tert*-butoxycarbonyl-L-tert-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 4-methylimidazole-5-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (180 mg, 78%). MS (ESI): 488.2 $(M+H)^+$.

Example 121

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-*tert*-butylalanyl)hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and picolinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.098 g, 62%). MS (ESI): 502.3 $(M+H)^+$.

Example 122

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b), the title compound was prepared as a white solid (0.083 g, 46%). MS (ESI): 552.2 $(M+H)^+$.

Example 123

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-allylglycinyl)hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-allylglycine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and

picolinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.141 g, 84%). MS (ESI): 472.2 $(M+H)^+$.

Example 124

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-cyclopropylalanyl)hydrazide

a) N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine methyl ester

To a stirring solution of the compound of Example 116(a) (7.81 g, 36.3 mmol) in ether (100 mL) at 0 °C was added a solution of diazomethane (made from 10 eq of 1-methyl-3-nitro-1-nitrosoguanidine in ether (500 mL) and 40% NaOH (500 mL) at 0 °C). After stirring for 10 min., $Pd(OAc)_2$ (0.300 g) was added to the solution. After 20 min., the solution was concentrated and the residue was filtered through a short plug of silica gel to remove unused catalyst. Concentration of the solution yielded the title compound as a golden yellow oil (8.29 g, 99%). ^1H NMR (400 MHz, $CDCl_3$) d 5.17 (d, 1H), 4.39 (m, 1H), 3.73 (s, 3H), 1.66 (t, 2H), 1.44 (s, 9H), 0.68 (m, 1H), 0.49 (m, 2H), 0.08 (m, 2H).

b) N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine

Following the procedure of Example 1(g), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine methyl ester for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a golden yellow oil (6.37 g, 82%). MS (ESI): 252.3 $(M+Na)^+$.

c) N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-cyclopropylalanyl)hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and picolinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.114 g, 71%). MS (ESI): 486.1 $(M+H)^+$.

Example 125

Preparation of N-[N-(6-methylnicotinoyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b)

and 6-methylnicotinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.097 g, 59%). MS (ESI): 500.1 $(M+H)^+$.

Example 126

Preparation of N-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 4-methylimidazole-5-carboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.095 g, 59%). MS (ESI): 489.1 $(M+H)^+$.

Example 127

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b), the title compound was prepared as a white solid (0.138 g, 78%). MS (ESI): 536.2 $(M+H)^+$.

Example 128

Preparation of N-[N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 6-methylnicotinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.124 g, 73%). MS (ESI): 516.1 $(M+H)^+$.

Example 129

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-*tert*-butylalanyl)hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-b-*tert*-butoxycarbonyl-L-tert-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a), the title compound was prepared as a white solid (143 mg, 83%). MS (ESI): 485.1 $(M+H)^+$.

Example 130

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-b-*tert*-butoxycarbonyl-L-tert-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 3-isoquinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (138 mg, 85%). MS (ESI): 535.1 $(M+H)^+$.

Example 131

Preparation of N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(a)-1(d) and 1(h), except substituting N-cyclopropylmethyl cyclopropylamine for cis-2,6-dimethylmorpholine in step (a) and N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as a white solid (1.375 g, 76%). MS (ESI): 464.2 $(M+H)^+$.

Example 132

Preparation of N-[2-(N-cyclopropylmethyl-N-propylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 1(a)-1(h), except substituting N-cyclopropyl propylamine for cis-2,6-dimethylmorpholine in step (a) and 6-methyl-3-pyridylcarbinol for 4-pyridylcarbinol in step (f), the title compound was prepared as an orange solid (84 mg, 33%). MS (ESI): 517.3 $(M+H)^+$.

Example 133

Preparation of N-[N-(6-methylnicotinoyl)-L-allylglycinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-allylglycine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 6-methylnicotinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared prepared as a white solid (0.097 g, 66%). MS (ESI): 486.1 $(M+H)^+$.

Example 134

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-allylglycinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-allylglycine for N-*tert*-butoxycarbonyl-L-leucine in step (b), the title compound was prepared as a white solid (0.105 g, 74%). MS (ESI): 522.1 $(M+H)^+$.

Example 135

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 2-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.151 g, 86%). MS (ESI): 536.3 $(M+H)^+$.

Example 136

Preparation of N-[N-(3-isoquinolinoyl)-L-b-cyclopropylalanyl]-N'-[-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 3-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.145 g, 82%). MS (ESI): 536.1 $(M+H)^+$.

Example 137

Preparation of N-[N-(1-isoquinolinoyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 1-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.143 g, 81%). MS (ESI): 536.1 $(M+H)^+$.

Example 138

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 7-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.138 g, 78%). MS (ESI): 536.1 $(M+H)^+$.

Example 139

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-

cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 8-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (120 mg, 73%). MS (ESI): 519.1 $(M+H)^+$.

Example 140

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 4-methylimidazole-5-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (120 mg, 81%). MS (ESI): 472.1 $(M+H)^+$.

Example 141

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 3-isoquinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared obtained as a white solid (140 mg, 82%). MS (ESI): 519.2 $(M+H)^+$.

Example 142

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 6-methylnicotinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (105 mg, 62%). MS (ESI): 483.2 $(M+H)^+$.

Example 143

Preparation of N-[N-(4-methylimidazol-5-ylcarbonyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 4-methylimidazole-5-carboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.112 g, 70%). MS (ESI): 491.1 $(M+H)^+$.

Example 144

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-norleucinyl)hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and picolinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.114 g, 72%). MS (ESI): 488.2 $(M+H)^+$.

Example 145

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-norleucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b), the title compound was prepared as a white solid (0.082 g, 47%). MS (ESI): 538.1 $(M+H)^+$.

Example 146

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 2-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (150 mg, 81%). MS (ESI): 519.2 $(M+H)^+$.

Example 147

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 1-isoquinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (130 mg, 87%). MS (ESI): 519.2 $(M+H)^+$.

Example 148

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide

Following the procedure of Example 1(a)-1(h), except substituting N-isobutyl cyclopropylamine for cis-2,6-dimethylmorpholine in step (a) and 6-methyl-3-pyridylcarbinol for 4-pyridylcarbinol in step (f), the title compound was prepared as a white solid (220 mg, 88%). MS (ESI): 517.2 $(M+H)^+$.

Example 149

Preparation of N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(a)-1(d) and 1(h), except substituting N-cyclopropyl isobutylamine for cis-2,6-dimethylmorpholine in step (a) and N-*tert*-butoxycarbonyl-L-leucine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as a white solid (1.01 g, 89%). MS (ESI): 466.3 $(M+H)^+$.

Example 150

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 7-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.139 g, 80%). MS (ESI): 552.2 $(M+H)^+$.

Example 151

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 2-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.158 g, 91%). MS (ESI): 552.2 $(M+H)^+$.

Example 152

Preparation of N-[N-(1-isoquinolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 1-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.143 g, 82%). MS (ESI): 552.2 $(M+H)^+$.

Example 153

Preparation of N-[N-(3-isoquinolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 3-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.130 g, 75%). MS (ESI): 552.2 $(M+H)^+$.

Example 154

Preparation of N-[N-(6-methylnicotinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 6-methylnicotinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.109 g, 67%). MS (ESI): 502.2 $(M+H)^+$.

Example 155

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-norleucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 7-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.104 g, 59%). MS (ESI): 538.1 $(M+H)^+$.

Example 156

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-norleucinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 2-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.153 g, 87%). MS (ESI): 538.1 $(M+H)^+$.

Example 157

Preparation of N-[N-(1-isoquinolinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 1-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.151 g, 86%). MS (ESI): 538.1 $(M+H)^+$.

Example 158

Preparation of N-[N-(3-isoquinolinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norleucine for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 3-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.126 g, 72%). MS (ESI): 538.1 $(M+H)^+$.

Example 159

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(5-hydroxymethylimidazol-4-ylcarbonyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 5-hydroxymehylimidazole-4-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (50 mg, 44%). MS (ESI): 488.2 $(M+H)^+$.

Example 160

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)- L-b-cyclopropylalanyl]hydrazide

a) N-(N-tert-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(a)-1(d) and 1(h), except substituting N-cyclopropyl isobutylamine for cis-2,6-dimethylmorpholine in step (a) and N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as a white solid (1.01 g, 89%). MS (ESI): 466.3 $(M+H)^+$.

b) N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)- L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 8-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (135 mg, 100%). MS (ESI): 521.2 $(M+H)^+$.

Example 161

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanyl)hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 6-methylnicotinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (85 mg, 79%). MS (ESI): 499.2 $(M+H)^+$.

Example 162

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)- L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 4-methylimidazole-5-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (100 mg, 73%). MS (ESI): 474.2 $(M+H)^+$.

Example 163

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)- L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 2-quinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (75 mg, 59%). MS (ESI): 521.2 $(M+H)^+$.

Example 164

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)- L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 6-methylnicotinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (112 mg, 65%). MS (ESI): 485.3 $(M+H)^+$.

Example 165

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)glycinyl]hydrazide

a) N-(8-quinolinoyl)glycine

Following the procedure of Example 102(f)-102(g), except substituting glycine methyl ester hydrochloride for L-leucine methyl ester in step (f), the title compound was prepared as a pale yellow solid (0.207 g, 95%). MS (ESI): 231.1 $(M+H)^+$.

b) N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)glycinyl]hydrazide

Following the procedure of Example 1(h), except substituting N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide and N-(8-quinolinoyl)glycine for N-(4-pyridylmethoxycarbonyl)-L-leucine, the title compound was prepared as a tan solid (0.028 g, 12%). MS (ESI): 482.1 $(M+H)^+$.

Example 166

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-norvalinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norvaline for N-*tert*-butoxycarbonyl-L-leucine in step (b), the title compound was prepared as a white solid (0.131 g, 74%). MS (ESI): 524.1 $(M+H)^+$.

Example 167

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-norvalinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norvaline for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 2-quinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.135 g, 75%). MS (ESI): 524.1 $(M+H)^+$.

Example 168

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-norvalinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norvaline for N-*tert*-butoxycarbonyl-L-leucine in step (b) and picolinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.126 g, 79%). MS (ESI): 474.2 $(M+H)^+$.

Example 169

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-norvalinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norvaline for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 6-methylnicotinic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.141 g, 85%). MS (ESI): 488.2 $(M+H)^+$.

Example 170

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-norvalinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norvaline for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 4-methylimidazole-5-carboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.098 g, 51%). MS (ESI): 477.1 $(M+H)^+$.

Example 171

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-norvalinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norvaline for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 1-

isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.146 g, 82%). MS (ESI): 524.2 $(M+H)^+$.

Example 172

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-norvalinyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting N-*tert*-butoxycarbonyl-L-norvaline for N-*tert*-butoxycarbonyl-L-leucine in step (b) and 3-isoquinolinecarboxylic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.138 g, 78%). MS (ESI): 524.2 $(M+H)^+$.

Example 173

Preparation of (1S, 1'S)-N, N'-bis-[4-[1-(N-benzyloxycarbonylamino)-3-methylbutyl]thiazol-2-ylcarbonyl]hydrazide

a) N-benzyloxycarbonyl-L-leucinamide

To a stirring solution of N-benzyloxycarbonyl-L-leucine (4.6 g, 17.3 mmol) in THF, cooled to -40 °C, was added N-methylmorpholine (3.68 g, 36.4 mmol; 4.0 mL) and isobutyl chloroformate (2.37 g, 17.3 mmol; 2.25 mL). After stirring for 15 min, ammonia was bubbled through the solution for 5 min. The solution was warmed to room temperature, evaporated, and the residue was dissolved in ethyl acetate, washed with 0.1 N Hcl, and saturated brine, then dried ($MgSO_4$), filtered and evaporated to dryness to give the title compound as a white solid (4.58 g, 100%).

b) N-benzyloxycarbonyl-L-leucinethioamide

A solution of the compound of Example 1(a) (4.58 g, 17.3 mmol) and Lawesson's reagent (4.21 g, 10.4 mmol) in THF was allowed to stir at room temperature for 16 h. The solution was concentrated and the residue was purified by flash chromatography on 230-400 mesh silica gel, eluting with 1:3 EtOAc/hexanes, to provide the title compound as a pale yellow solid (3.74 g, 77%).

c) (1S)-1-benzyloxycarbonylamino-1-(4-carboethoxythiazol-2-yl)-3-methylbutane

The compound of Example 1(b) (2.20 g, 7.83 mmol) was dissolved in acetone (35 mL), cooled to -10 °C, and ethyl bromopyruvate (1.68 g, 8.62 mmol, 1.08 mL) was added.

After stirring for 1 h, the solution was poured into methylene chloride/water, then into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with methylene chloride and the combined organic layers were washed with saturated brine, dried ($MgSO_4$), filtered and concentrated. The residue was dissolved in methylene chloride, cooled to -20 ° C, pyridine (1.36 g, 17.2 mmol, 1.39 mL) and trifluroracetic anhydride (1.81 g, 8.62 mmol, 1.22 mL) were added. After stirring for 1 h, the solution was washed with saturated squeous $NaHCO_3$ and saturated brine, then dired ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography on 90 g of 230-400 mesh silica gel, eluting with 1:3 ethyl acetate/hexanes, to provide the title compound as a pale yellow oil (2.36 g, 80%). ^1H NMR (400 MHz, $CDCl_3$) d 8.08 (s, 1H), 7.38 (m, 5H), 5.42 (s, 3H), 5.23-5.07 (m, 3H), 4.42 (q, 2H), 2.01-1.62 (m, 3H), 1.41 (t, 3H), 0.99 (d, 6H).

d) (1S)-1-benzyloxycarbonylamino-1-(4-hydrazinocarbonylthiazol-2-yl)-3-methylbutane

Following the procedure of Example 1(d), except substituting (1S)-1-benzyloxycarbonylamino-1-(4-carboethoxythiazol-2-yl)-3-methylbutane for ethyl 2-(cis-2,6-dimethyl-4-morpholino)thiazole-4-carboxylate, the title compound was prepared as a pale yellow foam (2.01 g, 97%). ^1H NMR (400 MHz, $CDCl_3$) d 8.35 (bs, 1H), 8.03 (s, 1H), 7.37 (m, 5H), 5.29 (d, 1H), 5.14-5.09 (m, 3H), 4.07 (bs, 2H), 1.92-1.82 (m, 1H), 1.79-1.66 (m, 2H), 1.00 (d, 6H).

e) (1S)-1-benzyloxycarbonylamino-1-(4-carboxythiazol-2-yl)-3-methylbutane

Following the procedure of Example 1(g), except substituting (1S)-1-benzyloxycarbonylamino-1-(4-carboethoxythiazol-2-yl)-3-methylbutane for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid. MS (ESI): 349.2 $(M+H)^+$.

f) (1S, 1'S)-N, N'-bis-[4-[1-(N-benzyloxycarbonylamino)-3-methylbutyl]thiazol-2-ylcarbonyl]hydrazide

Following the procedure of Example 1(h), except substituting (1S)-1-benzyloxycarbonylamino-1-(4-hydrazinocarbonylthiazol-2-yl)-3-methylbutane for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide and (1S)-1-benzyloxycarbonylamino-1-(4-carboxythiazol-2-yl)-3-methylbutane for N-(4-pyridylmethoxycarbonyl)-L-leucine, the title compound was prepared as a white solid (0.028 g, 59%). MS (ESI): 693.1 $(M+H)^+$.

Example 174

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]hydrazide

a) N-(N-tert-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 1(a)-1(d) and 1(h), except substituting N-cyclopropyl isobutylamine for cis-2,6-dimethylmorpholine in step (a) and N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanine for N-(4-pyridinylmethoxycarbonyl)-L-leucine in step (h), the title compound was prepared as a white solid (0.44 g, 100%). MS (ESI): 482.3 $(M+H)^+$.

b) N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 6-methylnicotinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (70 mg, 66%). MS (ESI): 501.2 $(M+H)^+$.

Example 175

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 4-methylimidazole-5-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (70 mg, 39%). MS (ESI): 490.2 $(M+H)^+$.

Example 176

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 1-isoquinolinecarboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (123 mg, 88%). MS (ESI): 535.3 $(M+H)^+$.

Example 177

Preparation of N-[N-(5-butylpicolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 5-butylpicolinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (90 mg, 85%). MS (ESI): 541.3 $(M+H)^+$.

Example 178

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylpicolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 6-methylpicolinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (170 mg, 86%). MS (ESI): 499.2 $(M+H)^+$.

Example 179

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-fluorobenzoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting 4-fluorobenzoic acid for picolinic acid in step (b), the title compound was prepared as a white solid (88 mg, 97%). MS (ESI): 488.2 $(M+H)^+$.

Example 180

Preparation of N-[N-(4-fluorobenzoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 59(a)-59(d), except substituting 4-fluorobenzoic acid for 8-quinolinecarboxylic acid in step (d), the title compound was prepared as a white solid (0.113 g, 69%). MS (ESI): 505.1 $(M+H)^+$.

Example 181

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]hydrazide

a) L-b-*tert*-butylalanine methyl ester hydrochloride

To a suspension of L-b-*tert*-butylalanine (2.0 g, 13.8 mmol) in 2,2-dimethoxypropane (75 mL) was added concentrated hydrochloric acid (12 mL). After standing at room temperature for 16 h, the solution was concentrated, redissolved in ethyl acetate and washed with 7.5% Na_2CO_3 (2 X). The organic layer was dried ($MgSO_4$), filtered and concentrated to yield the free base (1.3g, 8.2 mmol). This was dissolved in ether and HCl (8.2 mL, 1.0 M in ether) added. The white precipitate was collected by filtration yield the title compound as a white solid (1.32 g, 49%). MS (ESI): 159.7 $(M+H)^+$.

b) N-(2-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanine

Following the procedure of Example 1(e)-5(g), except substituting L-b-*tert*-butylalanine methyl ester hydrochloride for L-leucine methylo ester hydrochloride in step (e) and 2-pyridylcarbinol for 4-pyridylcarbinol in step (f), the title compound was prepared as a white solid (0.55 g, 100%). MS (ESI): 281.3 $(M+H)^+$.

c) N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 1(h), except substituting N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide for N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]hydrazide and N-(2-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanine for N-(4-pyridylmethoxycarbonyl)-L-leucine, the title compound was prepared as a white solid (0.155 g, 47%). MS (ESI): 532.2 $(M+H)^+$.

Example 182

Preparation of N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 181(a)-181(c), except substituting 2-methyl-3-pyridylcarbinol for 2-pyridylcarbinol in step (b), the title compound was prepared as a white solid (0.169 g, 67%). MS (ESI): 546.2 $(M+H)^+$.

Example 183

Preparation of N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]hydrazide

a) L-b-cyclopropylalanine methyl ester hydrochloride

Following the procedure of Example 181(a), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine methyl ester for L-b-*tert*-butylalanine, the title compound was prepared as a white solid (2.2 g, 30%). MS (ESI): 144.0 $(M+H)^+$.

b) N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 181(b)-181(c), except substituting L-b-cyclopropylalanine methyl ester hydrochloride for L-b-*tert*-butylalanine methyl ester hydrochloride in step (b), the title compound was prepared as a white solid (0.147 g, 61%). MS (ESI): 516.1 $(M+H)^+$.

Example 184

Preparation of N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 181(a)-181(c), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine methyl ester for L-b-*tert*-butylalanine in step (a) and 2-methyl-3-pyridylcarbinol for 2-pyridylcarbinol in step (b), the title compound was prepared as a white solid (0.159 g, 65%). MS (ESI): 530.2 $(M+H)^+$.

Example 185

Preparation of N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 181(a)-181(c), except substituting N-*tert*-butoxycarbonyl-L-b-cyclopropylalanine methyl ester for L-b-*tert*-butylalanine in step (a) and 6-methyl-3-pyridylcarbinol for 2-pyridylcarbinol in step (b), the title compound was prepared as a white solid (0.169 g, 69%). MS (ESI): 530.2 $(M+H)^+$.

Example 186

Preparation of N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 181(a)-181(c), except substituting 6-methyl-3-pyridylcarbinol for 2-pyridylcarbinol in step (b), the title compound was prepared as a white solid (0.194 g, 77%). MS (ESI): 546.2 $(M+H)^+$.

Example 187

Preparation of N,N'-bis-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide

a) ethyl 2-(1-naphthyl)thiazole-4-carbohydrazide

Following the procedure of Example 3(a)-3(c) and 3(e), except substituting 1-naphthylboronic acid for 4-methyl-1-naphthylboronic acid in step (e), the title compound was prepared as a pale yellow solid. MS (ESI): 270.1 $(M+H)^+$.

a) ethyl 2-(1-naphthyl)thiazole-4-carbohydrazide

Following the procedure of Example 1(g), except substituting ethyl 2-(1-naphthyl)thiazole-4-carbohydrazide for N-(4-pyridinylmethoxycarbonyl)-L-leucine methyl ester, the title compound was prepared as a white solid. MS (ESI): 256.0 $(M+H)^+$.

Example 188

Preparation of N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-[2-(1,8-naphthyridinoyl)]-L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 1,8-naphthyridine-2-carboxylic acid for picolinic acid in step (b), the title compound was prepared as a white solid (100 mg, 59%). MS (ESI): 520.2 $(M+H)^+$.

Example 189

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-difluorobenzoyl)- L-b-cyclopropylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-tert-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 3,4-difluorobenzoic acid for picolinic acid in step (b), the title compound was prepared as a white solid (208 mg, 100%). MS (ESI): 506.1 $(M+H)^+$.

Example 190

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-flluorobenzoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 4-fluorobenzoic acid for picolinic acid in step (b), the title compound was prepared as a white solid (130 mg, 70%). MS (ESI): 490.2 $(M+H)^+$.

Example 191

Preparation of N-[N-(5-butylpicolinoyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 5-butylpicolinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (100 mg, 63%). MS (ESI): 529.3 $(M+H)^+$.

Example 192

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-dimethoxybenzoyl)-L-leucinyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 3,4-dimethoxybenzoic acid for picolinic acid in step (b), the title compound was prepared as a white solid (130 mg, 84%). MS (ESI): 532.2 $(M+H)^+$.

Example 193

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-difluorobenzoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 3,4-difluorobenzoic acid for picolinic acid in step (b), the title compound was prepared as a white solid (120 mg, 78%). MS (ESI): 522.2 $(M+H)^+$.

Example 194

Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-dimethoxybenzoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 3,4-dimethoxybenzoic acid for picolinic acid in step (b), the title compound was prepared as a white solid (73 mg, 51%). MS (ESI): 546.3 $(M+H)^+$.

Example 195

Preparation of N-[N-(5-butylpicolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 5-butylpicolinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (120 mg, 77%). MS (ESI): 543.2 $(M+H)^+$.

Example 196

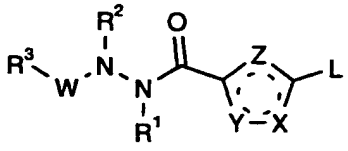
Preparation of N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylpicolinoyl)-L-b-*tert*-butylalanyl]hydrazide

Following the procedure of Example 56(a)-56(b), except substituting N-(N-*tert*-butoxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide for N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-*tert*-butoxycarbonyl-L-leucinyl)hydrazide in step (a) and 6-methylpicolinic acid for picolinic acid in step (b), the title compound was prepared as a white solid (104 mg, 72%). MS (ESI): 501.3 $(M+H)^+$.

The above specification and Examples fully disclose how to make and use the compounds of the present invention. However, the present invention is not limited to the particular embodiments described hereinabove, but includes all modifications thereof within the scope of the following claims. The various references to journals, patents and other publications which are cited herein comprise the state of the art and are incorporated herein by reference as though fully set forth.

We claim:

1. A compound of Formula I:



I

wherein:

L is C_{2-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, $CH(R^4)NR^5R^6$, $CH(R^4)Ar$, $CH(R^4)OAr'$, or NR^4R^7;

Ar is phenyl or naphthyl;

Ar' is phenyl or naphthyl;

Het is a stable 5- to 7-membered monocyclic or a stable 7- to 10-membered bicyclic heterocyclic ring, which is either saturated or unsaturated, and which consists of carbon atoms and from one to four heteroatoms selected from the group consisting of N, O and S, said heterocyclic ring being attached at any heteroatom or carbon atom which results in a stable structure, or any bicyclic group in which any of said monocyclic heterocyclic rings is fused to a benzene ring;

W is C(O), SO_2;

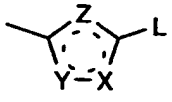
X, Y, and Z are independently N, O, S or CR^{10},

provided that at least two of X, Y and Z are heteroatoms and at least one of X, Y and Z is N, or that one of X, Y and Z is C=N, C=C or N=N and the other two are CR^{10} or N, further provided that at least two of X, Y and Z are N;

= indicates a single or double bond in the five-membered heterocycle;

R', R^1, R^2, R^5, R^8, R^9, R^{10}, and R^{12} are independently H, C_{1-6}alkyl, C_{2-6}alkenyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R^3 is C_{3-6}alkyl, Ar, Het, $CH(R^{11})Ar$, $CH(R^{11})OAr$, $NR^{11}R^{12}$, $CH(R^{11})NR^{12}R^{13}$; or



;

R^4, R^{11}, and R^{15} are independently H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-6}cycloalkyl-C_{0-6}-alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R^7 is C_{1-6}alkyl, C_{1-6}alkenyl, C_{3-6}cycloalkyl-C_{0-6}-alkyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl;

R^6 and R^{13} are R^{14}, $R^{14}C(O)$, $R^{14}C(S)$, $R^{14}OC(O)$, or $R^{14}OC(O)NR^9CH(R^{15})(CO)$; and

R^{14} is C_{1-6}alkyl, C_{2-6}alkenyl, Ar-C_{0-6}alkyl, or Het-C_{0-6}alkyl.

and pharmaceutically acceptable salts, hydrates and solvates thereof.

2. A compound according to Claim 1 wherein Ar is independently substituted by one or more moieties selected from the group consisting of: Ph-C_{0-6}alkyl, Het-C_{0-6}alkyl, C_{1-6}alkyl, C_{1-6}alkoxy, Ph-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', or halogen.

3. A compound according to Claim 2 wherein Ph is independently substituted by one or more moieties selected from the group consisting of: C_{1-6}alkyl, C_{1-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', and halogen.

4. A compound according to Claim 2 wherein two C_{1-6}alkyl groups are combined to form a 5-7 membered ring, saturated or unsaturated, fused onto the Ar ring.

5. A compound according to Claim 1 wherein Ar' is independently substituted by one or more moieties selected from the group consisting of: Ph-C_{0-6}alkyl, Het-C_{0-6}alkyl, C_{1-6}alkyl, C_{1-6}alkoxy, Ph-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', or halogen.

6. A compound according to Claim 5 wherein Ph is independently substituted by one or more moieties selected from the group consisting of: C_{1-6}alkyl, C_{1-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', and halogen.

7. A compound according to Claim 5 wherein two C_{1-6}alkyl groups are combined to form a 5-7 membered ring, saturated or unsaturated, fused onto the Ar' ring.

8. A compound according to Claim 1 wherein Het is independently substituted with one or two moieties selected from the group consisting of: Ph-C_{0-6}alkyl, Het-C_{0-6} alkyl, C_{1-6}alkyl, C_{1-6}alkoxy, Ph-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, or CO_2R'.

9. A compound according to Claim 8 wherein Ph is independently substituted by one or more moieties selected from the group consisting of: C_{1-6}alkyl, C_{1-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, $O(CH_2)_{1-6}NR^8R^9$, CO_2R', and halogen.

10. A compound according to Claim 8 wherein two C_{1-6}alkyl groups are combined to form a 5-7 membered ring, saturated or unsaturated, fused onto the Het ring.

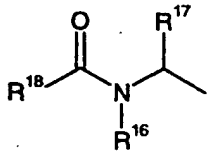
11. A compound according to Claim 1 wherein Het is selected from the group consisting of the piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, triazolyl, tetrazolyl, pyridyl, pyrazinyl, pryidazinyl, pyrimidinyl, triazinyl, tetrazinyl, oxazolidinyl, oxazolinyl, oxazolyl, isothiazolyl, isoxazolyl, morpholinyl, thiazolidinyl, thiazolinyl, thiazolyl, quinuclidinyl, indolyl, quinolinyl, isoquinolinyl, benzimidazolyl, benzopyranyl, benzoxazolyl, furyl, pyranyl, tetrahydrofuryl, tetrahydropyranyl, thienyl, benzoxazolyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, thiadiazolyl, and oxadiazolyl rings.

12. A compound according to Claim 1 wherein R^4 and R^7 may be combined to form a 3-7 membered monocyclic or 7-10-membered bicyclic carbocyclic or heterocyclic ring.

13. A compound according to Claim 12 wherein said 3-7 membered monocyclic or 7-10-membered bicyclic carbocyclic or heterocyclic ring is independently substituted with 1-4 moieties selected from the group consisting of: C_{1-6}alkyl, Ar-C_{0-6}alkyl, Het-C_{0-6}alkyl, C_{1-6}alkoxy, Ar-C_{0-6}alkoxy, Het-C_{0-6}alkoxy, OH, $(CH_2)_{1-6}NR^8R^9$, and $O(CH_2)_{1-6}NR^8R^9$.

14. A compound according to Claim 1 wherein Z = N, X = S, and Y = CH.

15. A compound according to Claim 14 wherein R^3 is further defined as:



wherein:

R^{16} is H or C_{1-6}alkyl;

R^{17} is C_{1-6}alkyl, C_{2-6}alkenyl, or C_{3-11}cycloalkyl; and

R^{18} is C_{3-6}alkyl, OC_{3-6}alkyl, Ar, Het, $O(CH_2)_{0-3}$Ar, or $O(CH_2)_{0-3}$Het.

16. A compound according to Claim 15 wherein R^{16} is H or Me.

17. A compound according to Claim 15 wherein R^{17} is *n*-propyl, *iso*-propyl, *iso*-pentyl, *tert*-butylmethyl, cyclopropylmethyl, *iso*-butyl, *n*-butyl, or allyl.

18. A compound according to Claim 15 wherein R^{18} is selected from the group consisting of: 2-pyridinylmethoxy, 3-pyridinylmethoxy, 4-pyridinylmethoxy, *tert*-butoxy, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-pyrazinyl, 4-*tert*-butoxycarbonylbenzyloxy, 4-carboxybenzyloxy, 3-*tert*-butoxycarbonylbenzyloxy, 3-carboxybenzyloxy, 2-methyl-3-pyridinylmethoxy, 6-methyl-3-pyridinylmethoxy, benzyloxy, 2-quinolino, 3-quinolino, 4-quinolino, 5-quinolino, 6-quinolino, 7-quinolino, 8-quinolino, 1-isoquinolino, 3-isoquinolino, piperidinyl, 4-methylpiperidinyl, 4-methylimidazol-5-yl, N-benzyl-pyrrolidinyl, N-methyl-pyrrolidinyl, 1-benzyl-5-methylimidazol-4-yl, 1-piperazinyl; 3-(2-pyridyl)benzyl, 2-methyl-3-pyridinyl, 2-methyl-4-pyridinyl, 6-methyl-3-pyridinyl, 4-dimethylaminobenzyloxy, 4-(4-morpholinomethyl)phenyl, 5-hydroxymethylimidazol-4-yl, 5-butyl-2-pyridinyl, 4-fluorophenyl, 3,4-difluorophenyl, 2-(1,8-naphthyridinyl), or 3,4-dimethoxyphenyl.

19. A compound according to Claim 14 wherein L is selected from the group consisting of: 4-(cis-2,6-dimethyl)-4-morpholinyl, N-cyclopropylmethyl-N-(2-methylpropyl)amino, 4-methyl-1-naphthyl, N-methyl-N-(2-methylpropyl)amino, 1-naphthyl, 5-acenaphthyl, N-cyclopropyl-N-cyclopropylmethylamino, N,N-bis-(2-methylpropyl)amino, 1-(1,2,3,4-tetrahydroquinolino, N-cyclopropylmethyl-N-propylamino, N-(2-methylpropyl)-N-phenylamino, 2-methoxy-1-naphthyl, 2-benzyloxyphenyl, 2-benzyloxy-1-naphthyl, 9-phenanthrenyl, 9-anthracenyl, phenyl, 2-(4-*tert*-butoxycarbonyl)benzyloxyphenyl, 2-(4-carboxybenzyloxy)phenyl, N-cyclopropylamino, 8-quinolino, N,N-bis-(cyclopropylmethyl)amino, 4-(2,2-dimethylaminoethoxy)-1-naphthyl, or 1-(N-benzyloxycarbonylamino)-3-methylbutyl.

20. A compound according to Claim 1 selected from the group consisting of: N-[2-(cis-2,6-dimethyl-4-morpholino)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(4-methyl-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(5-acenaphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-[1-(1,2,3,4-tetrahydroquinolino)]thiazol-4-ylcarbonyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[4-methyl-2-(3-phenyl)phenylpent-4-enoyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropylmethyl-N-propylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[4-methyl-2-(3-phenyl)phenylpentanoyl]hydrazide;

N-[N-(2-methylpropyl)-N-(3-phenylphenyl)carbamoyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[4-methyl-2-(3-phenyl)phenylpentanoyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[4-methyl-2-(3-phenyl)phenylpentanoyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-[2-(2-methoxy-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[4-methyl-2-(3-phenyl)phenylpentanoyl]hydrazide;

N-[2-(2-benzyloxy-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(9-phenanthrenyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(9-anthracenyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-(-*tert*-butoxycarbonyl-L-leucinyl)ydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(L-leucinyl)]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyrazinecarbonyl)-L-leucinyl]hydrazide;

N-[N,N-bis-(2-methylpropyl)carbamoyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-(2-phenylthiazol-4-ylcarbonyl)-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[2-(4-*tert*-butoxycarbonyl)benzyloxyphenyl]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[2-(4-carboxybenzyloxy)phenyl]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-carboxybenzyloxycarbonyl)-L-leucinyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycaronyl-L-leucinyl)-N'-[2-[2-(4-*tert*-butoxycarbonyl)benzyloxyphenyl]thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycaronyl-L-leucinyl)-N'-[2-[2-(4-carboxybenzyloxy)phenyl]thiazol-4-ylcarbonyl]hydrazide;

N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-()-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(3-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;
N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;
N-[N-(3-carboxybenzyloxycarbonyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-leucinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-quinolinoyl)-L-leucinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-methylpiperidinecarbonyl)-L-leucinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-quinolinoyl)-L-leucinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(5-quinolinoyl)-L-leucinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-leucinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(6-quinolinoyl)-L-leucinyl]hydrazide;
N-[N-(1-isoquinolinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(3-isoquinolinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(4-methylimidazol-5-ylcarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-(N-benzyl-L-prolinyl-L-leucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(1-benzyl-5-methylimidazol-4-ylcarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(3-methylisonicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(N-cyclopropylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[4-methyl-2-(3-phenoxy)phenylpentanoyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(2-benzoxazolyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-[N,N-bis-(2-methylpropyl)amino]oxazol-4-ylcarbonyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(1-piperazinecarbonyl)-L-leucinyl]hydrazide;

N-[4-methyl-2-(4-phenoxy)phenylpentanoyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-leucinyl]hydrazide;

N-[N-(8-quinolinoyl)-L-leucinyl]-N'-[2-(8-quinolinyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-(N-benzyloxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-[3-(2-pyridyl)phenylacetyl]-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-picolinyl-L-leucinyl)hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-methylnicotinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-methylisonicotinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-leucinyl]hydrazide;

N-[2-[4-(2,2-dimethylaminoethoxy)-1-naphthyl]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-methyl-L-prolinyl-L-leucinyl)hydrazide;

N-(N-benzyloxycarbonyl-L-norvalinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-isoleucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(4-dimethylaminomethylbenzoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-norleucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(4-dimethylaminomethylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-norvalinyl)-N'-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-leucinyl]hydrazide;

N-[N-[4-(4-morpholinomethyl)benzoyl]-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(2-methylnicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(6-methylnicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-b-*tert*-butoxycarbonyl-L-*tert*-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[N-(4-methylimidazol-5-ylcarbonyl)-L-allylglycinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-*tert*-butylalanyl)hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-allylglycinyl)hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-cyclopropylalanyl)hydrazide;
N-[N-(6-methylnicotinoyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;
N-[N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-*tert*-butylalanyl)hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(N-cyclopropylmethyl-N-propylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[N-(6-methylnicotinoyl)-L-allylglycinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-allylglycinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;
N-[N-(3-isoquinolinoyl)-L-b-cyclopropylalanyl]-N'[-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(1-isoquinolinoyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-cyclopropylalanyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-b-cyclopropylalanyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-b-cyclopropylalanyl]hydrazide;
N-[N-(4-methylimidazol-5-ylcarbonyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-norleucinyl)hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-norleucinyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-b-cyclopropylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[N-(1-isoquinolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(3-isoquinolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(6-methylnicotinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-norleucinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-norleucinyl]hydrazide;
N-[N-(1-isoquinolinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(3-isoquinolinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(5-hydroxymethylimidazol-4-ylcarbonyl)-L-b-cyclopropylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)glycinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-norvalinyl]hydrazide;

(1S, 1'S)-N, N'-bis-[4-[1-(N-benzyloxycarbonylamino)-3-methylbutyl]thiazol-2-ylcarbonyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[N-(5-butylpicolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylpicolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-fluorobenzoyl)-L-leucinyl]hydrazide;

N-[N-(4-fluorobenzoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]hydrazide;
N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N,N'-bis-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-[2-(1,8-naphthyridinoyl)]-L-b-cyclopropylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-difluorobenzoyl)- L-b-cyclopropylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-flluorobenzoyl)-L-leucinyl]hydrazide;
N-[N-(5-butylpicolinoyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-dimethoxybenzoyl)-L-leucinyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-difluorobenzoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-dimethoxybenzoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[N-(5-butylpicolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide; and
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylpicolinoyl)-L-b-*tert*-butylalanyl]hydrazide.

21. A compound according to Claim 20 which is selected from the group consisting of:

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-(4-methyl-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;
N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(5-acenaphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropylmethyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-[1-(1,2,3,4-tetrahydroquinolino)]thiazol-4-ylcarbonyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropylmethyl-N-propylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxy-1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(9-phenanthrenyl)thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-(-*tert*-butoxycarbonyl-L-leucinyl)ydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyrazinecarbonyl)-L-leucinyl]hydrazide;

N-[2-[2-(4-*tert*-butoxycarbonyl)benzyloxyphenyl]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[2-(4-carboxybenzyloxy)phenyl]thiazol-4-ylcarbonyl]-N'-[N-(4-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-[2-[N,N-bis-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(4-carboxybenzyloxycarbonyl)-L-leucinyl]-N'-[2-[N-(2-methylpropyl)-N-phenylamino]thiazol-4-ylcarbonyl]hydrazide;

N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-methyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-()-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(3-*tert*-butoxycarbonylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;

N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-leucinyl)hydrazide;

N-[N-(3-carboxybenzyloxycarbonyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-methylpiperidinecarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(5-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(6-quinolinoyl)-L-leucinyl]hydrazide;

N-[N-(1-isoquinolinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(3-isoquinolinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(4-methylimidazol-5-ylcarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(1-benzyl-5-methylimidazol-4-ylcarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(3-methylisonicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-[N,N-bis-(2-methylpropyl)amino]oxazol-4-ylcarbonyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-methyl-N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(1-piperazinecarbonyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-leucinyl]hydrazide;

N-[N-(8-quinolinoyl)-L-leucinyl]-N'-[2-(8-quinolinyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-(N-benzyloxycarbonyl-L-b-*tert*-butylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-[3-(2-pyridyl)phenylacetyl]-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-picolinyl-L-leucinyl)hydrazide;

N-(N-benzyloxycarbonyl-L-leucinyl)-N'-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-methylisonicotinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-leucinyl]hydrazide;

N-[2-[4-(2,2-dimethylaminoethoxy)-1-naphthyl]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-leucinyl]hydrazide;

N-[2-[N-bis-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-(N-methyl-L-prolinyl-L-leucinyl)hydrazide;

N-(N-benzyloxycarbonyl-L-norvalinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-isoleucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-norleucinyl)-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(4-dimethylaminomethylbenzyloxycarbonyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-benzyloxycarbonyl-L-norvalinyl)-N'-[2-(2-benzyloxyphenyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-leucinyl]hydrazide;

N-[N-[4-(4-morpholinomethyl)benzoyl]-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(6-methylnicotinoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-(N-b-*tert*-butoxycarbonyl-L-*tert*-butylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[N-(4-methylimidazol-5-ylcarbonyl)-L-allylglycinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-*tert*-butylalanyl)hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-allylglycinyl)hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-cyclopropylalanyl)hydrazide;

N-[N-(6-methylnicotinoyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-b-*tert*-butylalanyl)hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-(N-*tert*-butoxycarbonyl-L-b-cyclopropylalanyl)-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropylmethyl-N-propylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-[N-(6-methylnicotinoyl)-L-allylglycinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-allylglycinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[N-(3-isoquinolinoyl)-L-b-cyclopropylalanyl]-N'[-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(1-isoquinolinoyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[N-(4-methylimidazol-5-ylcarbonyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-norleucinyl)hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-norleucinyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-leucinyl]hydrazide;

N-(N-*tert*-butoxycarbonyl-L-leucinyl)-N'-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[N-(1-isoquinolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(3-isoquinolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(6-methylnicotinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(7-quinolinoyl)-L-norleucinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-norleucinyl]hydrazide;

N-[N-(1-isoquinolinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[N-(3-isoquinolinoyl)-L-norleucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(5-hydroxymethylimidazol-4-ylcarbonyl)-L-b-cyclopropylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-(N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)- L-b-cyclopropylalanyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)glycinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(8-quinolinoyl)-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-quinolinoyl)-L-norvalinyl]hydrazide;

N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-(N-picolinoyl-L-norvalinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-norvalinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-norvalinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-norvalinyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(3-isoquinolinoyl)-L-norvalinyl]hydrazide;
(1S, 1'S)-N, N'-bis-[4-[1-(N-benzyloxycarbonylamino)-3-methylbutyl]thiazol-2-ylcarbonyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylnicotinoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-methylimidazol-5-ylcarbonyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(1-isoquinolinoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[N-(5-butylpicolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(6-methylpicolinoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-(4-fluorobenzoyl)-L-leucinyl]hydrazide;
N-[N-(4-fluorobenzoyl)-L-leucinyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(1-naphthyl)thiazol-4-ylcarbonyl]-N'-[N-(2-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]hydrazide;
N-[N-(2-methyl-3-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-b-cyclopropylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[N-(6-methyl-3-pyridinylmethoxycarbonyl)-L-b-*tert*-butylalanyl]-N'-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N,N'-bis-[2-(1-naphthyl)thiazol-4-ylcarbonyl]hydrazide;
N-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]-N'-[N-[2-(1,8-naphthyridinoyl)]-L-b-cyclopropylalanyl]hydrazide;

N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-difluorobenzoyl)- L-b-cyclopropylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(4-flluorobenzoyl)-L-leucinyl]hydrazide;
N-[N-(5-butylpicolinoyl)-L-leucinyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-dimethoxybenzoyl)-L-leucinyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-difluorobenzoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(3,4-dimethoxybenzoyl)-L-b-*tert*-butylalanyl]hydrazide;
N-[N-(5-butylpicolinoyl)-L-b-*tert*-butylalanyl]-N'-[2-(N-cyclopropyl-N-cyclopropylmethylamino)thiazol-4-ylcarbonyl]hydrazide; and
N-[2-[N-cyclopropyl-N-(2-methylpropyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methylpicolinoyl)-L-b-*tert*-butylalanyl]hydrazide.

22. A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier, diluent or excipient.

23. A pharmaceutical composition comprising a compound according to Claim 21 and a pharmaceutically acceptable carrier, diluent or excipient.

24. A method of inhibiting a protease selected from the group consisting of a cysteine protease and a serine protease, comprising administering to a patient in need thereof an effective amount of a compound according to Claim 1.

25. A method of inhibiting a protease selected from the group consisting of a cysteine protease and a serine protease, comprising administering to a patient in need thereof an effective amount of a compound according to Claim 21.

26. A method according to Claim 24 wherein said protease is a cysteine protease.

27. A method according to Claim 25 wherein said protease is a cysteine protease.

28. A method according to Claim 26 wherein said cysteine protease is cathepsin K.

29. A method according to Claim 27 wherein said cysteine protease is cathepsin K.

30. A method of treating a disease characterized by bone loss comprising inhibiting said bone loss by administering to a patient in need thereof an effective amount of a compound according to Claim 1.

31. A method according to Claim 30 wherein said disease is osteoporosis.

32. A method according to Claim 30 wherein said disease is periodontitis.

33. A method according to Claim 30 wherein said disease is gingivitis.

34. A method of treating a disease characterized by excessive cartilage or matrix degradation comprising inhibiting said excessive cartilage or matrix degradation by administering to a patient in need thereof an effective amount of a compound according to Claim 1.

35. A method according to Claim 34 wherein said disease is osteoarthritis.

36. A method according to Claim 34 wherein said disease is rheumatoid arthritis.

37. A method of treating a disease characterized by bone loss comprising inhibiting said bone loss by administering to a patient in need thereof an effective amount of a compound according to Claim 21.

38. A method according to Claim 37 wherein said disease is osteoporosis.

39. A method according to Claim 37 wherein said disease is periodontitis.

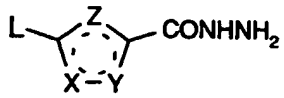
40. A method according to Claim 37 wherein said disease is gingivitis.

41. A method of treating a disease characterized by excessive cartilage or matrix degradation comprising inhibiting said excessive cartilage or matrix degradation by administering to a patient in need thereof an effective amount of a compound according to Claim 21.

42. A method according to Claim 41 wherein said disease is osteoarthritis.

43. A method according to Claim 41 wherein said disease is rheumatoid arthritis.

44. A method for preparing compounds according to Claim 1, comprising the step of reacting an intermediate:

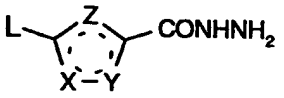


with a carboxylic acid, R^3CO_2H, and a peptide coupling reagent in an aprotic solvent.

45. A method according to Claim 44 wherein said peptide coupling reagent is EDC•HCl/1-HOBT when a carboxylic acid is used.

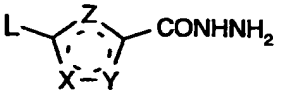
46. A method according to Claim 45 wherein said aprotic solvent is DMF.

47. A method for preparing compounds according to Claim 1, comprising the step of reacting an intermediate:



with a carbamoyl chloride, R^3COCl, and triethylamine in methylene chloride.

48. A method for preparing compounds according to Claim 1, comprising the step of reacting an intermediate:



with a sulfonyl chloride, R^3SO_2Cl, and NMM in CH_2C1_2.

49. Use of a compound according to any one of claims 1 to 21 in the manufacture of a medicament for use in inhibiting a protease selected from the group consisting of a cysteine protease and a serine protease.

50. A use according to Claim 49 wherein said protease is a cysteine protease.

51. A use according to Claim 51 wherein said cysteine protease is cathepsin K.

52. Use of a compound according to any one of claims 1 to 21 in the manufacture of a medicament for use in treating a disease characterized by bone loss.

53. A use according to Claim 52 wherein said disease is osteoporosis.

54. A use according to Claim 52 wherein said disease is periodontitis.

55. A use according to Claim 52 wherein said disease is gingivitis.

56. Use of a compound according to any one of claims 1 to 21 in the manufacture of a medicament for use in treating a disease characterized by excessive cartilage or matrix degradation.

57. A use according to Claim 56 wherein said disease is osteoarthritis.

58. A use according to Claim 56 wherein said disease is rheumatoid arthritis.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/08740

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AFRIDI, A. S. et al. Heterocyclic Rearrangements. Part XIV. Attempts to Activate Ring-Opening-Ring-Closure Rearrangements with Carbon as the Central Atom. J.C.S. Perkin Trans I, 1976, Vol. 3, pages 315-320, especially page 317.	1
X	KOSARY, J. et al. Synthesis of Pyridylthiazoles as Antisecretory Agents. Pharmazie. March 1989, Vol. 44, No. 3, pages 191-193, especially page 192.	1, 11, 22
X	SRIDEVI, G. et al. Some Reactions and Rearrangements of Isoxazol-3-Carbonyl Azides and Hydrazides. Indian Journal of Chemistry. February 1990, Vol. 29B, No. 2, pages 182-183, especially page 182.	1-2

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 16 JULY 1998	Date of mailing of the international search report 24 AUG 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Cynthia Lawrence for BRENDA COLEMAN Telephone No. (703) 308-1235

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/08740

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	THOMPSON, S.K. et al. Design of Potent and Selective Human Cathepsin K Inhibitors That Span the Active Site. Proceedings of the National Academy of Sciences. 23 December 1997, Vol. 94, No. 26, pages 14249-14254, especially page 14250.	1-58
X,P	WO 97/16433 A1 (SMITHKLINE BEECHAM CORPORATION) 09 May 1997, see entire document.	1-58

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/08740

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

A61K 31/41, 31/415, 31/42, 31/425, 31/495, 31/50, 31/505, 31/53, 31/555; C07D 231/04, 231/06, 231/10, 233/02, 233/04, 233/54, 233/96, 237/00, 237/02, 239/02, 241/02, 249/08, 251/00, 253/00, 257/08, 257/12, 261/04, 261/08, 263/04, 263/08, 263/30, 271/06, 271/10, 273/01, 275/02, 277/04, 277/08, 277/20, 285/00, 285/08, 285/12, 291/04, 403/02, 403/04, 403/14, 405/02, 405/14, 407/02, 407/14,409/02, 409/14, 411/02, 411/14, 413/02, 413/14, 417/02, 417/14, 419/02, 419/14

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

514/183, 241, 242, 252, 253, 254, 255, 256, 359, 360, 362, 363, 364, 365, 372, 374, 378, 383, 385, 397, 400, 401, 402, 403, 406; 544/179, 182, 215, 224, 238, 295, 296, 333, 335, 357, 405, 406; 548/122, 123, 124, 128, 131, 136, 143, 200, 214, 215, 237, 238, 240, 248, 255, 266.2, 266.4, 266.6, 266.8, 311.1, 311.4, 311.7, 312.1, 312.4, 312.7, 313.1, 313.4, 314.4, 314.7, 315.1, 315.4, 333.5, 356.1, 364.1, 364.4, 364.7, 365.1, 365.4, 365.7, 374.1, 379.4

B. FIELDS SEARCHED
Minimum documentation searched
Classification System: U.S.

514/183, 241, 242, 252, 253, 254, 255, 256, 359, 360, 362, 363, 364, 365, 372, 374, 378, 383, 385, 397, 400, 401, 402, 403, 406; 544/179, 182, 215, 224, 238, 295, 296, 333, 335, 357, 405, 406; 548/122, 123, 124, 128, 131, 136, 143, 200, 214, 215, 237, 238, 240, 248, 255, 266.2, 266.4, 266.6, 266.8, 311.1, 311.4, 311.7, 312.1, 312.4, 312.7, 313.1, 313.4, 314.4, 314.7, 315.1, 315.4, 333.5, 356.1, 364.1, 364.4, 364.7, 365.1, 365.4, 365.7, 374.1, 379.4